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SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF MIZOLASTINE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Mizolastine is an antihistamine drug. Three simple, sensitive and accurate spectrophotometric methods have been developed for the determination of mizolastine in pure state and in its pharmaceutical dosage forms. The method A is based on the complex formation of the drug with cobalt thiocyanate and the developed chromogen in method A exhibits maximum absorption at λ_{max} 620 nm and linearity in the range of 20-100 µg/mL. The developed method B is based on ion association complex formation between the drug and methyl orange to produce colored chromogen having maximum absorption at λ_{max} 420 nm. Beer's law is obeyed in the range of 10-50 µg/mL. Method C is based on ion association complex formation of the drug with bromothymol blue to form colored chromogen and it shows maximum absorption at λ_{max} 415 nm and linearity in the range of 2-10 µg/mL. Results of analysis were validated statistically and by recovery studies.

Key words: Mizolastine, Spectrophotometric.

INTRODUCTION

Mizolastine[1] 2-[[1-[1-[(4-fluorophenyl) methyl] benzimidazol-2-yl] piperidin-4-yl]-methylamino]-1H-pyrimidin-6-one (MZL) is a new benzimidazole derivative drug, which is a potent and selective antagonist of H1 receptors. Mizolastine blocks histamine H1 receptors and is commonly fast acting. It does not prevent the actual release of histamine from mast cells, but just prevents its binding to receptors.

Literature survey reveals the pharmacokinetic study of MZL by liquid-liquid extraction[2], LC-ESI-MS method for the determination of mizolastine in human plasma[3], coupled liquid-liquid extraction and column switching LC for the determination of a new

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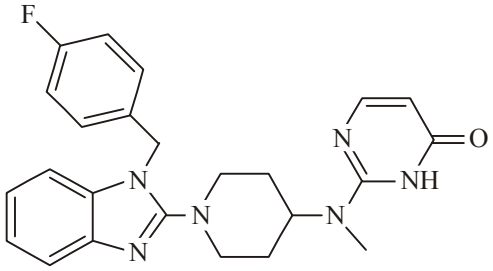
antihistaminic H1 drug in human urine[4], Development of a CZE method for the determination of mizolastine and its impurities in pharmaceutical preparations using response surface methodology[5] and spectrophotometric determination of mizolastine in pharmaceutical formulations[6] were reported. In the present investigation, three simple, sensitive and accurate visible spectrophotometric methods have been developed for the estimation of mizolastine in pharmaceutical dosage forms and in bulk drug. Method A shows λ_{max} at 620 nm and linearity in the range of 20-100 µg/mL. Method B exhibits λ_{max} at 420 nm and linearity in the range of 10-50 µg/mL. Method C shows λ_{max} at 415 nm and linearity in the range of 2-10 µg/mL.



Structure of mizolastine

EXPERIMENTAL

Spectral and absorbance measurements were made on Systronics double beam UV-Visible spectrophotometer Model 2201 with 1 cm matched quartz cells. Mizolastine was procured from a local pharmaceutical industry. All other reagents used were of analytical grade.

Reagents preparation

For Method A, Cobalt thiocyanate (2.5×10^{-1} M)

7.25 g of cobaltous nitrate and 3.8 g of ammonium thiocyanate were dissolved in 100 mL of distilled water.

For Method B, Methyl orange (0.1%)

100 mg of methyl orange was dissolved in 100 mL of distilled water.

Acid phthalate buffer pH 4

To 50 mL of potassium hydrogen phthalate solution, 0.1 mL of HCl was added and

made up to 200 mL with distilled water.

Potassium hydrogen phthalate (0.2M)

40.846 g of potassium hydrogen phthalate was dissolved in 1000 mL of distilled water.

For Method C, Bromothymol blue

200 mg of bromothymol blue was initially dissolved in minimum amount of 0.1 N NaOH and further diluted to 100 mL with distilled water.

Buffer pH 2.0

It was prepared by mixing 50 mL of 0.1 M glycine solution with 50 mL of 0.1 M HCl solution and the pH was adjusted to 2.

M Glycine solution

About 0.75 g of glycine was dissolved in 100 mL of water.

Standard preparation

For method A, about 100 mg of pure MZL was accurately weighed and dissolved in 100 mL of chloroform to get 1 mg/mL stock solution. The solution itself can be used as working standard for method A.

For methods B and C, about 100 mg of MZL was accurately weighed and dissolved in 100 mL of 0.1 N HCl to get 1 mg/mL stock solution. The solution itself can be used as working standard for method B. From the stock solution, 10 mL of the drug was taken and further diluted to 100 mL to get 100 μg/mL which can be used as working standard for method C.

Preparation of sample solution

For method A, the powder equivalent to 100 mg was taken in a 100 mL volumetric flask and it was extracted with 100 mL of chloroform to get 1 mg/mL stock solution. This can be used as such for method A. For methods B and C, the powder equivalent to 100 mg was taken in a 100 mL volumetric flask and extracted with 0.1 N HCl to get the stock solution of concentration 1 mg/mL. This can be used as such for method B. From this, 10

mL was taken and further diluted to 100 mL with 0.1 N HCl to get the working standard solution of concentration 100 µg/mL for method C.

Procedure for estimation

Method A: Into a series 25 mL separating funnels, aliquots of standard solution of drug containing 20-100 µg (0.2-1.0 mL) from 1 mg/mL stock solution was taken and it was equalized with chloroform. To each funnel, 4 mL of pH 2 buffer and 4 mL of cobalt thiocyanate were added. It was then extracted with 10 mL of nitrobenzene. The absorbance was measured at 620 nm against a reagent blank. The amount of MZL in sample was calculated from the Beer-Lambert's plot.

Methods B and C : Into a series 25 mL separating funnels, aliquots of standard MZL solution of concentration of 1 mg/mL containing 10-50 µg (0.1-0.5 mL) for Method B and with a concentration of 100 µg/mL containing 2-10 µg (0.2-1.0 mL) for Method C were transferred and equalized with 0.1 N HCl. To this, 5.0 mL acid phthalate buffer of pH 4 and 2.0 mL of methyl orange were added and it was made up to 10 mL with water for method B. 8.0 mL of glycine buffer of pH 2 and 5.0 mL of bromothymol blue solution were added and it was made up to 15 mL with water for method C. Then it was extracted with 10 mL chloroform for method B and with benzene for method C and dried over anhydrous sodium sulphate. The absorbances were measured at 420 nm for method B and 415 nm for method C against reagent blank. The amount of MZL in sample was calculated from Beer-Lambert's plot.

RESULTS AND DISCUSSION

The proposed method A is based on the blue colored complex formed between mizolastine and cobalt thiocyanate can be attributed to presence of cyclic tertiary nitrogen in mizolastine.

The proposed methods B and C are based on the drug, which possesses cyclic tertiary nitrogen. It forms ion association complex with acidic dyes methyl orange and bromothymol blue, which is extractable into chloroform from the aqueous solution. The protonated nitrogen (positive charge) of MZL molecule in acid medium is expected to attract the oppositely charged part (negative charge) of the dye and behave as a single unit being held together by electrostatic attraction. The slope ratio method of study revealed that the drug to dye ratio as 1 : 1.

The interference studies revealed that the common excipients usually present in the dosage forms do not interfere in the proposed method.

The optical characteristics and validation parameters are given in Table 1. To evaluate the accuracy and reproducibility of the method, known amounts of the pure drug was added to the previously analyzed pharmaceutical formulations and the mixtures were reanalyzed by the proposed methods. The recoveries (average of six determinations) are given in Table 2.

Table 1: Optical characteristics, regression data, precision and accuracy of the proposed methods for mizolastine

Parameter	Method A	Method B	Method C
λ_{max} (nm)	620	420	415
Beer's law limits (μg/mL)	20-100	10-50	2-10
Molar absorptivity (Lit.mole^{-1}.cm^{-1})	3.43 x 10^3	4.72 x 10^3	2.83 x 10^4
Detection limits (μg/mL)	2.68	1.09	0.174
Sandell's Sensitivity (μg/cm^2/0.001 abs. unit)	0.1257	0.091463	0.01526
Optimum photometric range	19.5-99.5	9.5-49.5	1.5-9.5
Regression equation (Y = a + bc)			
Slope (b)	0.007755	0.01098	0.0651
Standard deviation of slope (Sb)	9.51 x 10^{-5}	5.18 x 10^{-5}	5.67 x 10^{-4}
Intercept (a)	0.0129	-0.002238	-0.00133
Standard deviation of intercept (Sa)	6.313 x 10^{-3}	1.57 x 10^{-3}	3.43 x 10^{-3}
Standard error of estimation (Se)	6.01 x 10^{-3}	2.16 x 10^{-3}	4.74 x 10^{-3}
Correlation coefficient (r)	0.9995	0.9999	0.9997
% Relative standard deviation*	0.3647	0.2727	0.4011
% Range of error* (confidence limits) 0.05 level	0.0935	0.0716	0.0839
0.01 level	0.1229	0.0941	0.1103
% Error in bulk samples**	0.2	-0.31	0.01

*Average of six determinations
**Average of three determinations

The values obtained for the determination of mizolastine in several pharmaceutical formulations (tablets) and bulk drug by the proposed and reference methods were compared (Table 2).The results indicate that the proposed methods are simple, sensitive, accurate and reproducible and can be used for the routine determination of mizolastine in bulk and pharmaceutical dosage forms.

Table 2: Assay and recovery of mizolastine in dosage forms

Method	Pharmaceutical formulation	Labelled amount (mg)	Proposed method			Found by reference method ± S.D	% Recovery by proposed methods** ± S.D
			Amount found* (mg) ± S.D	t (value)	F (value)		
A	Tablet-I	10	10.07 ± 0.010	0.704	2.531	10.12 ± 0.015	99.98 ± 0.37
	Tablet -II	10	10.12 ± 0.015	0.713	1.233	9.93 ± 0.006	99.95 ± 0.28
B	Tablet -I	10	9.93 ± 0.006	0.572	1.341	10.02 ± 0.011	100.12 ± 0.42
	Tablet -II	10	9.78 ± 0.005	0.61	1.564	9.97 ± 0.013	98.78 ± 0.45
C	Tablet -I	10	10.06 ± 0.013	0.534	1.249	9.99 ± 0.009	101.12 ± 0.19
	Tablet -II	10	10.11 ± 0.010	0.621	2.584	10.06 ± 0.018	100.12 ± 0.81

*Average ± Standard deviation of six determinations, the t and F values refer to comparison of the proposed method with reference method.
Theoretical values at 95 % confidence limits t = 2.571 and F = 5.05
**Average of five determinations

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